

WHAT IS CLAIMED IS:

1. A method for coupling a highly phosphorylated mannopyranosyl oligosaccharide compound to a glycoprotein having at least one glycan, or to chemical compounds with a carbonyl group, said method comprising:

derivatizing the highly phosphorylated mannopyranosyl oligosaccharide compound with a chemical compound containing a carbonyl-reactive group;

oxidizing the glycoprotein having at least one glycan to generate at least one carbonyl (aldehyde) group on the glycoprotein; and

reacting the oxidized glycoprotein having at least one glycan, or a chemical compound with a carbonyl group, with the derivatized highly phosphorylated mannopyranosyl oligosaccharide compound to form a new compound having a hydrazone bond.

2. A method in accordance with Claim 1 wherein oxidizing the glycoprotein having at least one glycan comprises oxidizing the glycoprotein with one of periodate or galactose oxidase.

3. A method in accordance with Claim 1 wherein the glycoprotein having the at least one glycan comprises a lysosomal enzyme.

4. A method in accordance with Claim 3 wherein the glycoprotein comprises a lysosomal enzyme is isolated from a natural source or produced in a recombinant expression system.

5. A method in accordance with Claim 1 wherein the highly phosphorylated mannopyranosyl oligosaccharide compound contains at least one mannose 6-phosphate group.

6. A method in accordance with Claim 5 wherein the highly phosphorylated mannopyranosyl oligosaccharide compound comprises a compound having the formula 6-P-M_n-R wherein:

M is a mannose or mannopyranosyl group;

P is a phosphate group linked to the C-6 position of M;

R comprises a chemical group containing a carbonyl-reactive group, and

n is an integer from 1-15, wherein if $n > 1$, M_n are linked to one another by alpha (1,2), alpha (1,3), alpha (1,4), or alpha (1,6).

7. A method in accordance with Claim 6 wherein the highly phosphorylated mannopyranosyl oligosaccharide compound comprises one of M6P, phosphopentamannose derived from *Hansenula holstii* O-phosphomannan, and 6-P-M-(alpha 1,2)-M(alpha 1,2)-M.

8. A method in accordance with Claim 5 wherein the highly phosphorylated mannopyranosyl oligosaccharide compound comprises a compound having the formula $(6-P-M_x)_m L_n-R$ wherein:

M is a mannose or mannopyranosyl group;

L is a mannose or other hexose or other chemical groups;

P is a phosphate group linked to the C-6 position of M;

R comprises a chemical group containing a carbonyl-reactive group;

m is an integer from 2-3;

n is an integer from 1-15, wherein if $n > 1$, M_n are linked to one another by alpha (1,2), alpha (1,3), alpha (1,4), or alpha (1,6); and

x is an integer from 1-15.

9. A method in accordance with Claim 8 wherein the highly phosphorylated mannopyranosyl oligosaccharide compound comprises a biantennary mannopyranosyl oligosaccharide compound containing bis-M6P or a triantennary mannopyranosyl oligosaccharide compound containing bis-M6P or tri-M6P.

10. A method in accordance with Claim 1 wherein the highly phosphorylated mannopyranosyl oligosaccharide compound can be substituted with oligosaccharides containing other terminal hexoses.

11. A method in accordance with Claim 10 wherein the terminal hexose is a galactose, a mannose, N-acetylglucosamine, and a fucose.

12. A method in accordance with Claim 1 wherein the chemical compound containing the carbonyl-reactive groups is a chemical compound that react with carbonyl groups to form a hydrazone bond.

13. A method in accordance with Claim 12 wherein the chemical compound containing carbonyl-reactive groups comprises a hydrazine, a hydrazide, an aminooxyl, or a semicarbozide compound or others.

14. A method in accordance with Claim 1 further comprising reducing the compound having a hydrazone bond with a reducing agent to form a compound having an imine bond.

15. A method in accordance with Claim 14 wherein the reducing agent comprises a cyanoborohydride compound.

16. A chemical compound in accordance with Claim 1 comprising coupling a first chemical compound having a carbonyl group, according to the method of Claim 1, to a second chemical compound comprising a phosphorylated mannopyranosyl oligosaccharide derivative.

17. A chemical compound in accordance with Claim 16 wherein the first chemical compound having at least one carbonyl group comprises an anti-viral agent.

18. A chemical compound in accordance with Claim 16 wherein the first chemical compound having at least one carbonyl group comprises a gene target delivery agent.

19. A chemical compound in accordance with Claim 18 wherein the gene targeting delivery agent comprises polycations, cationic lipids or oligonucleotides.

20. A method of treating a lysosomal storage disease in a subject in need thereof, said method comprising administering to the subject an effective amount of a glycoprotein coupled according to the method of Claim 1 to a second chemical compound comprising a highly phosphorylated mannopyranosyl oligosaccharide derivative containing at least one mannose 6-phosphate group.

21. A method in accordance with Claim 20 wherein the glycoprotein is a lysosomal enzyme and the lysosomal storage disease is selected from the group

consisting of Fabry disease, Pompe disease, Hurler or Hurler-Scheie disease, Krabbe disease, Metachromatic leukodystrophy, Hunter disease, Sanfilippo A and B disease, Morquio A disease, Maroteaux-Lamy disease and Gaucher disease.